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L4 HAS NO ANSWERS
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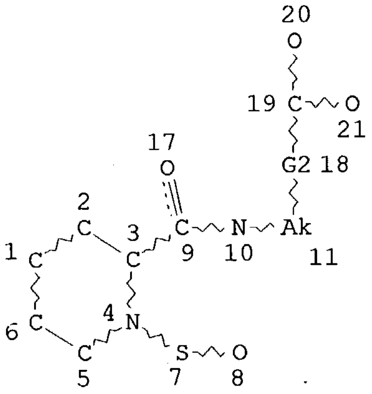

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE


=> s l4 ful
FULL SEARCH INITIATED 16:59:24 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  12306 TO ITERATE

100.0% PROCESSED   12306 ITERATIONS                          36 ANSWERS
SEARCH TIME: 00.00.03

L6            36 SEA SSS FUL L4

=> fil caplus
COST IN U.S. DOLLARS                               SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                    317.32     317.53

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FILE COVERS 1907 - 7 Dec 2004  VOL 141 ISS 24
FILE LAST UPDATED: 6 Dec 2004  (20041206/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l6
L7          11 L6

=> d bib abs hitstr 1-11

L7   ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:892751  CAPLUS
DN   139:381384
TI   Preparation of 2,6-quinolinyl and 2,6-naphthyl(acylamino)propionic acids
     as VLA-4 inhibitors
IN   Lassoie, Marie-Agnes; Knerr, Laurent; Demaude, Thierry; De Laveleye,
     Francoise; Kogej, Thierry; Routier, Sylvain; Guillaumet, Gerald
PA   UCB, S.A., Belg.
SO   PCT Int. Appl., 122 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE       APPLICATION NO.       DATE
     ---------------     ----   --------   --------------------  --------
PI   WO 2003093237        A1    20031113   WO 2003-EP3909        20030415
        W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
            PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
            TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI EP 2002-9746         A     20020430
OS   MARPAT 139:381384
GI
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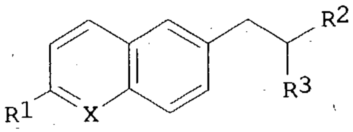

I

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AB   Title compds. I [ X = N, CH; R1 = R1 = cycloalkyl, aryl, hewterocyclic,
     heterocyclylalkyl, substituted OH, norbornen-5-yl; R2 = (un)substituted
     NH2, OH, CONH2; R3 = tetrazolyl, CN, CH2OH, (un)substituted CO2H] were
     prepared for use in treating VLA-4 dependent inflammatory diseases such as
     asthma, allergic rhinitis, sinusitis, conjunctivitis, food allergy,
     psoriasis, urticaria, pruritus, eczema, rheumatoid arthritis, inflammatory
     bowel disease, multiple sclerosis and atherosclerosis (no data).  Thus,
     4-nitrophenylalanine was esterified, N-protected , reduced to the amine,
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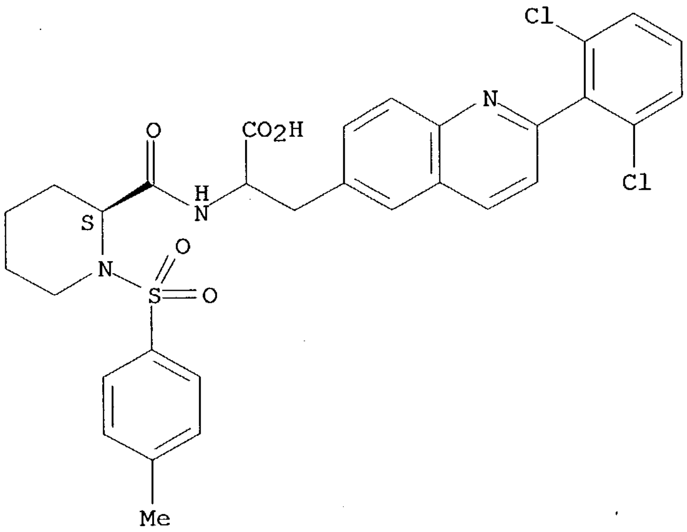
cyclized with 2,6-Cl2C6H3CHO and CH2:CHSPh, followed by elimination of PhSH to give I [X = N, R1 = 2,6-Cl2C6H3, R2 = NHBoc, R3 = CO2Me]. This compound was deprotected and acylated with 2,6-Cl2C6H3COCl, followed by ester hydrolysis to give I [X = N, R1 = 2,6=Cl2C6H3, R2 = 2,6-Cl2C6H3CONH, R3 = CO2H].

IT **623144-86-5P 623145-20-0P 623145-21-1P**
623145-31-3P 623145-36-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2,6-quinolinyl and 2,6-naphthyl(acylamino)propionic acids as VLA-4 inhibitors)

RN 623144-86-5 CAPLUS

CN 6-Quinolinepropanoic acid, 2-(2,6-dichlorophenyl)-α-[[[(2S)-1-[(4-methylphenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]- (9CI) (CA INDEX NAME)

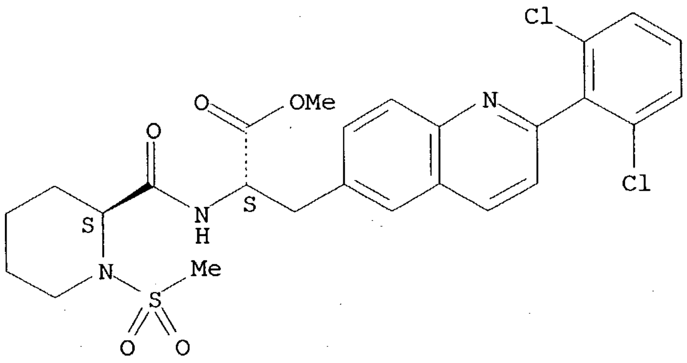
Absolute stereochemistry.



RN 623145-20-0 CAPLUS

CN 6-Quinolinepropanoic acid, 2-(2,6-dichlorophenyl)-α-[[[(2S)-1-(methylsulfonyl)-2-piperidinyl]carbonyl]amino]-, methyl ester, (αS)-(9CI) (CA INDEX NAME)

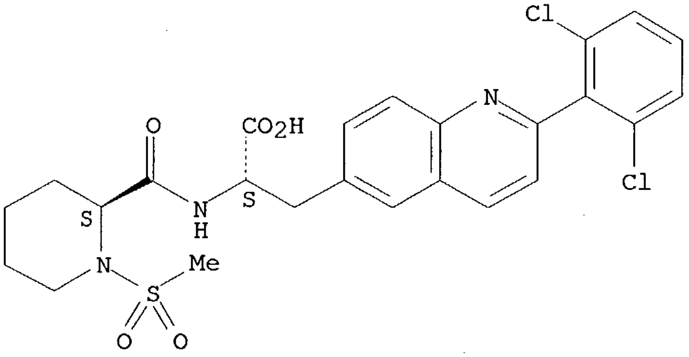
Absolute stereochemistry.



RN 623145-21-1 CAPLUS

CN 6-Quinolinepropanoic acid, 2-(2,6-dichlorophenyl)-α-[[[(2S)-1-(methylsulfonyl)-2-piperidinyl]carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

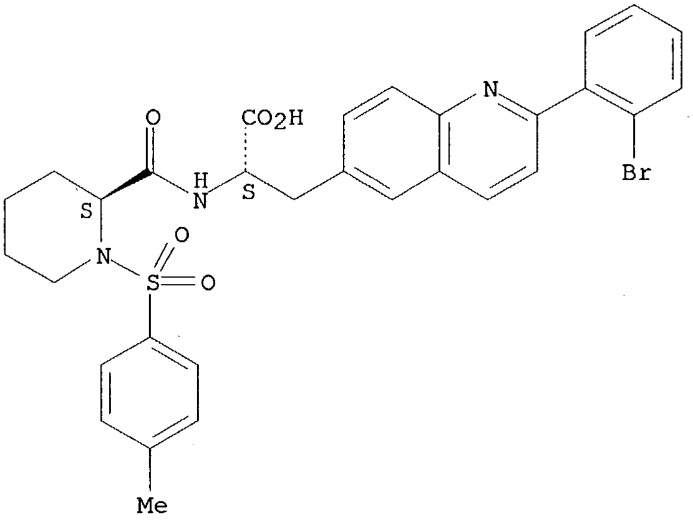
Absolute stereochemistry.



RN 623145-31-3 CAPLUS

CN 6-Quinolinepropanoic acid, 2-(2-bromophenyl)-α-[[[(2S)-1-[(4-methylphenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

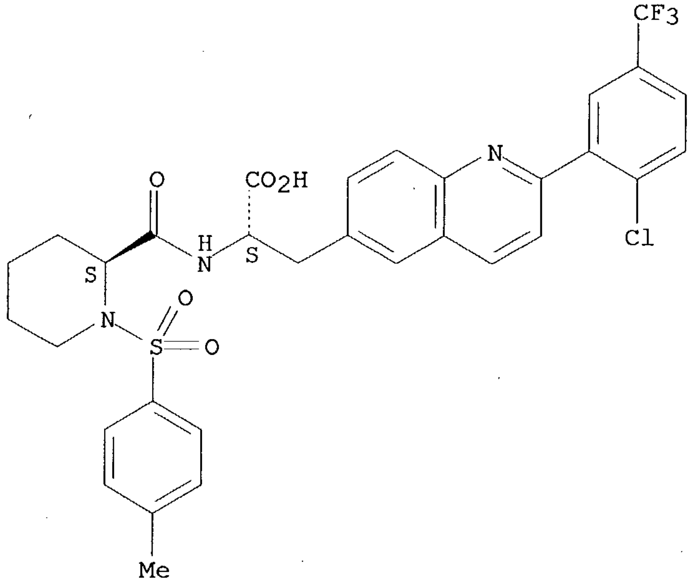
Absolute stereochemistry.



RN 623145-36-8 CAPLUS

CN 6-Quinolinepropanoic acid, 2-[2-chloro-5-(trifluoromethyl)phenyl]-α-[[[(2S)-1-[(4-methylphenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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RE.CNT  7       THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
                ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7    ANSWER 2 OF 11  CAPLUS  COPYRIGHT 2004 ACS on STN
AN    2003:887675  CAPLUS
DN    139:381751
TI    Preparation of substituted β-alanine derivatives as cell adhesion
      inhibitors
IN    Durette, Philippe L.; Hagmann, William K.; Kopka, Ihor E.; MacCoss,
      Malcolm; Mills, Sander G.; Mumford, Richard A.; Magriotis, Plato A.
PA    Merck & Co., Inc., USA
SO    U.S., 45 pp., Cont.-in-part of U.S. Ser. No. 198,680, abandoned.
      CODEN: USXXAM
DT    Patent
LA    English
FAN.CNT 3
      PATENT NO.          KIND  DATE          APPLICATION NO.       DATE
      ---------------     ----  --------      --------------------  --------
PI    US 6645939           B1   20031111      US 1999-317789        19990524
      WO 2000071572        A1   20001130      WO 2000-US14017       20000519
          W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
              CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
              ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
              MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE,
              SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
              ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
              CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1997-66484P        P    19971124
     US 1998-198680        B2   19981124
     US 1999-317789        A2   19990524
OS   MARPAT 139:381751
GI
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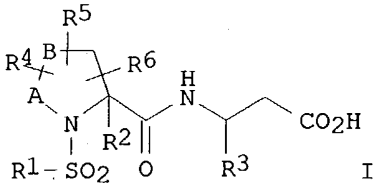


I

AB β-Alanine derivs. I [A = C; B = a bond, O, S, CH2; R1 = Ph optionally substituted by 1 or 2 halo, alkoxy, or trifluoromethyl groups; R2 = H, Me; R3 = (un)substituted (hetero)aryl, (hetero)aryl-(hetero)aryl; R4, R5, R6 = H, alkyl, halo] were prepared as antagonists of VLA-4 and/or α4β7 and as such are useful in the inhibition or prevention of cell adhesion and cell-adhesion mediated pathologies. Thus, N-[(3,4-dimethoxybenzenesulfonyl)-1,2,3,4-tetrahydroisoquinoline-3(S)-carbonyl]-3(S)-(3,4-methylenedioxyphenyl)-3-aminopropionic acid was prepared by amidation of N-(tert-butoxycarbonyl)-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid with Me (S)-3-amino-3-(3,4-methylenedioxyphenyl)propanoate, deblocking, sulfonylation with 3,4-dimethoxybenzenesulfonyl chloride, and saponification

IT **225515-74-2P 225516-38-1P**

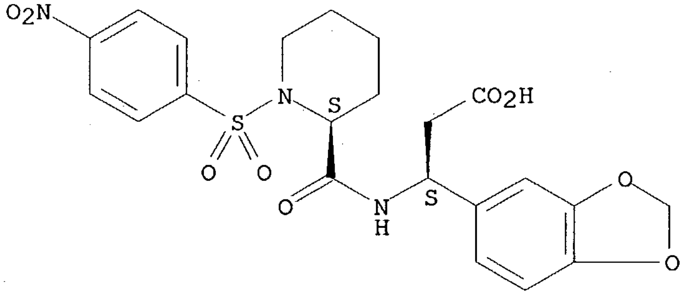
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted β-alanine derivs. as cell adhesion inhibitors)

RN 225515-74-2 CAPLUS

CN 1,3-Benzodioxole-5-propanoic acid, β-[[[(2S)-1-[(4-nitrophenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]-, (βS)- (9CI) (CA INDEX NAME)

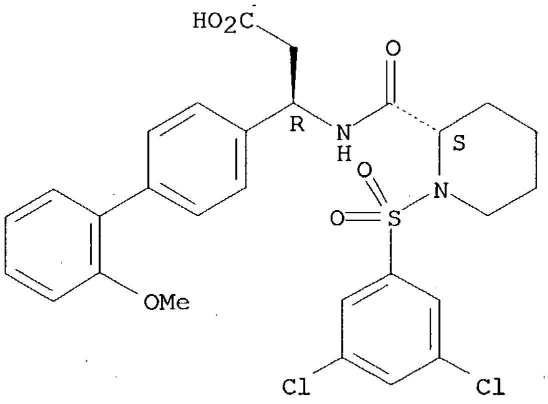
Absolute stereochemistry.



RN 225516-38-1 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, β-[[[(2S)-1-[(3,5-dichlorophenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]-2'-methoxy-, (βR)- (9CI) (CA INDEX NAME)

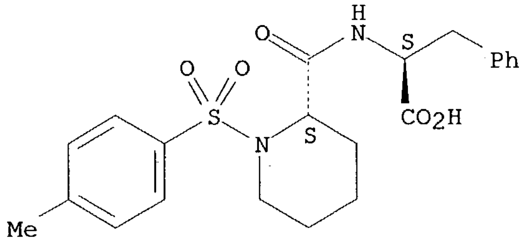
Absolute stereochemistry.



RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:162668 CAPLUS
DN 139:78416
TI Peptidyl aldehyde inhibitors of calpain incorporating P2-proline mimetics
AU Donkor, Isaac O.; Korukonda, Rajani; Huang, Tien L.; LeCour, Louis
CS Department of Pharmaceutical Sciences, University of Tennessee Health Science Center, Memphis, TN, 38163, USA
SO Bioorganic & Medicinal Chemistry Letters (2003), 13(5), 783-784
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 139:78416
AB Four new peptidyl aldehydes bearing proline mimetics at the P2-position were synthesized and studied as inhibitors of calpain I, cathepsin B, and selected serine proteases. The ring size of the P2-constraining residue influenced the inhibitory potency and selectivity of the compds. for calpain I compared to the other proteases.
IT **220186-90-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptidyl aldehyde inhibitors of calpain incorporating P2-proline mimetics)
RN 220186-90-3 CAPLUS
CN L-Phenylalanine, N-[[(2S)-1-[(4-methylphenyl)sulfonyl]-2-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L7   ANSWER 4 OF 11  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:76750  CAPLUS
DN   138:137595
TI   Preparation of N-[(aryl or thienyl)sulfonyl]dipeptide derivatives and
     analogs as α2β1 integrin inhibitors
IN   Takayanagi, Masaru; Fukuchi, Naoyuki; Sugiki, Masayuki; Futaki, Fumie;
     Takehana, Shunji; Kajigaya, Yuki; Takamatsu, Yayoi; Tokumasu, Munetaka;
     Yoshida, Kaoru
PA   Ajinomoto Co., Inc., Japan
SO   PCT Int. Appl., 187 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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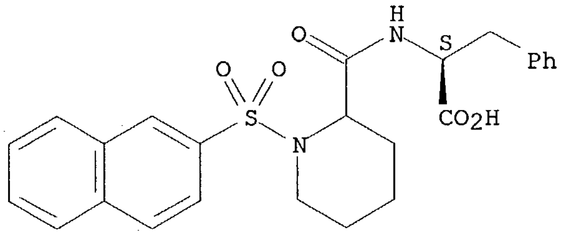
PI   WO 2003008380        A1    20030130    WO 2002-JP7250         20020717
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRAI JP 2001-218507       A     20010718
     JP 2001-351077       A     20011116
OS   MARPAT 138:137595
AB   The compds. represented by the following formula D-Y-N(L)-CH(B)-X-
     CH[(CH2)nA]COE [wherein n = an integer of 0-2; X = CH2O, CO2, each
     N-(un)substituted CH2NH, CONH, C(S)NH, or SO2NH, CH2S, CH2SO2; Y = CH2,
     CO, C(S), SO2, each N-(un)substituted NHCO or NHC(S); A, D =
     (un)substituted Ph, aryl, heteroaryl; B = (un)substituted amino-lower
     alkyl or carbamoyl-lower alkyl; L = H, lower alkyl, lower alkenyl, lower
     alkynyl, cycloalkyl or cycloalkyl-lower alkyl optionally containing a
     heteroatom in the ring, aryl, heteroaryl, aryl-lower alkyl,
     heteroaryl-lower alkyl, halo-lower alkyl, hydroxy-lower alkyl, lower
     alkoxy-lower alkyl, mercapto-lower alkyl, lower alkylthio-lower alkyl,
     (un)substituted amino-lower alkyl, carboxy-lower alkyl, lower
     alkoxycarbonyl-lower alkyl, (un)substituted carbamoyl-lower alkyl; E = HO,
     lower alkoxy, (un)substituted amino, hydroxylamino] or pharmacol.
     acceptable salts thereof are prepared  These compds. have α2β1
     integrin inhibitory activity (inhibition of binding between platelet
     GPIa/IIa receptor and collagen) and are useful as antiplatelet agents for
     the prevention or treatment of various diseases such as myocardial
     infarction, angina pectoris, acute coronary syndrome, peripheral artery
     obstruction, deep venous thrombosis, cerebral infarction, stroke, and
     pulmonary embolism.  Thus, N-(4-nitrobenzenesulfonyl)-L-prolyl-L-4-
     aminophenylalanine (prepared by the Fmoc solid phase method) showed IC50 of
     2.0 μg/mL for inhibiting the binding of collagen to platelet GPIa/IIa
     receptor.
IT   493040-51-0P 493040-52-1P 493040-53-2P
     493040-54-3P 493040-63-4P 493040-64-5P
     493041-11-5P 493041-12-6P 493041-13-7P
     493041-14-8P 493041-15-9P 493044-87-4P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
```

(preparation of N-[(aryl or thienyl)sulfonyl]dipeptide derivs. and analogs as α2β1 integrin inhibitors and antiplatelet agents for the prevention or treatment of various diseases)

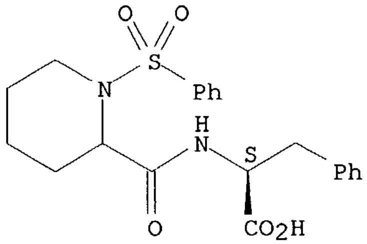
RN 493040-51-0 CAPLUS
CN L-Phenylalanine, N-[[1-(2-naphthalenylsulfonyl)-2-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



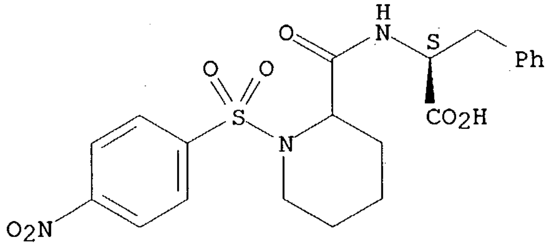
RN 493040-52-1 CAPLUS
CN L-Phenylalanine, N-[[1-(phenylsulfonyl)-2-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



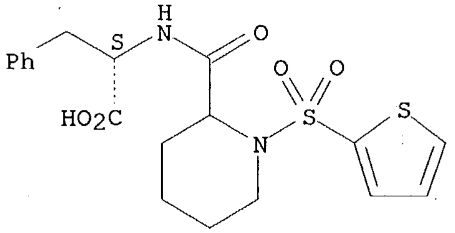
RN 493040-53-2 CAPLUS
CN L-Phenylalanine, N-[[1-[(4-nitrophenyl)sulfonyl]-2-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



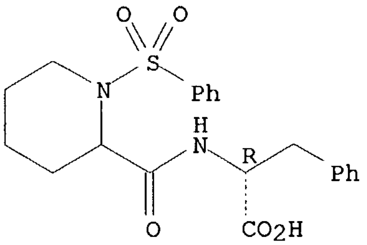
RN 493040-54-3 CAPLUS
CN L-Phenylalanine, N-[[1-(2-thienylsulfonyl)-2-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



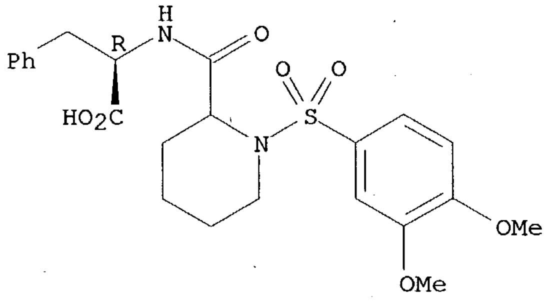
RN   493040-63-4   CAPLUS
CN   D-Phenylalanine, N-[[1-(phenylsulfonyl)-2-piperidinyl]carbonyl]- (9CI)
      (CA INDEX NAME)

Absolute stereochemistry.



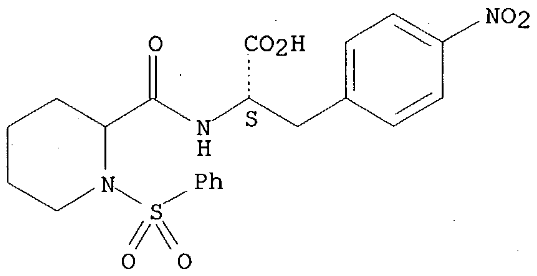
RN   493040-64-5   CAPLUS
CN   D-Phenylalanine, N-[[1-[(3,4-dimethoxyphenyl)sulfonyl]-2-
      piperidinyl]carbonyl]- (9CI)   (CA INDEX NAME)

Absolute stereochemistry.



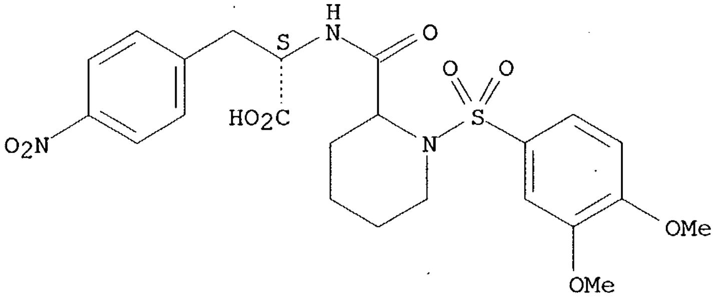
RN   493041-11-5   CAPLUS
CN   L-Phenylalanine, 4-nitro-N-[[1-(phenylsulfonyl)-2-piperidinyl]carbonyl]-
      (9CI)   (CA INDEX NAME)

Absolute stereochemistry.



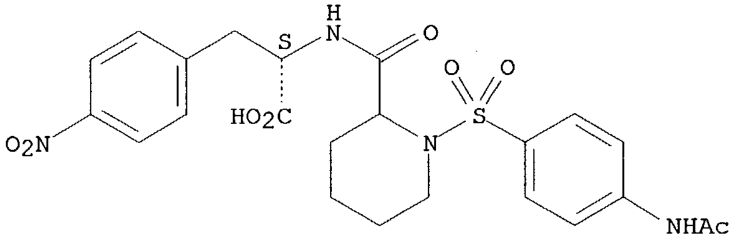
RN 493041-12-6 CAPLUS
CN L-Phenylalanine, N-[[1-[(3,4-dimethoxyphenyl)sulfonyl]-2-piperidinyl]carbonyl]-4-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



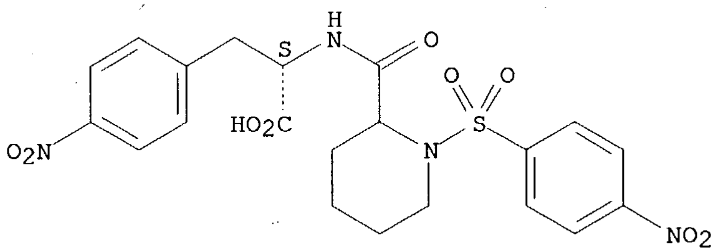
RN 493041-13-7 CAPLUS
CN L-Phenylalanine, N-[[1-[[4-(acetylamino)phenyl]sulfonyl]-2-piperidinyl]carbonyl]-4-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



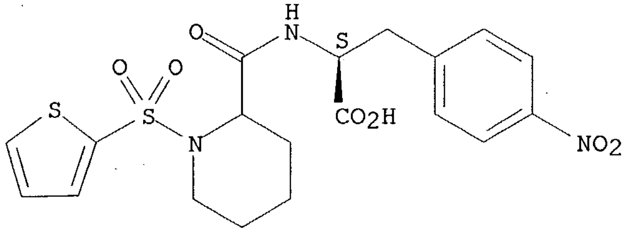
RN 493041-14-8 CAPLUS
CN L-Phenylalanine, 4-nitro-N-[[1-[(4-nitrophenyl)sulfonyl]-2-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 493041-15-9 CAPLUS
CN L-Phenylalanine, 4-nitro-N-[[1-(2-thienylsulfonyl)-2-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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RN    493044-87-4  CAPLUS
CN    Benzenebutanoic acid, α-[[[1-[(4-nitrophenyl)sulfonyl]-2-
      piperidinyl]carbonyl]amino]-, (αS)- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
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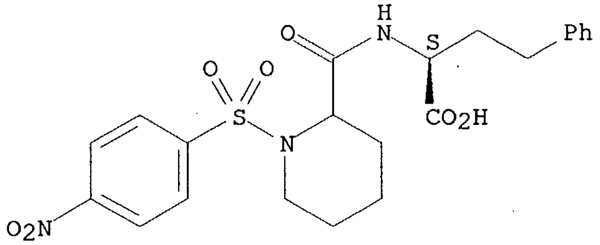

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RE.CNT  29     THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7    ANSWER 5 OF 11  CAPLUS  COPYRIGHT 2004 ACS on STN
AN    2001:137020  CAPLUS
DN    134:193741
TI    Preparation of peptide derivatives as cell adhesion inhibitors
IN    Lee, Wen-Cherng; Scott, Daniel; Cornebise, Mark; Petter, Russell
PA    Biogen, Inc., USA
SO    PCT Int. Appl., 144 pp.
      CODEN: PIXXD2
DT    Patent
LA    English
FAN.CNT 1
      PATENT NO.          KIND   DATE        APPLICATION NO.       DATE
      ---------------     ----   --------    --------------------  --------
PI    WO 2001012186        A1    20010222    WO 2000-US22285       20000814
          W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
              HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
              LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
              SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
              YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
              CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
      CA 2380817           AA    20010222    CA 2000-2380817       20000814
      BR 2000013248        A     20020723    BR 2000-13248         20000814
      EP 1265606           A1    20021218    EP 2000-959232        20000814
          R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO, MK, CY, AL
      JP 2003506491        T2    20030218    JP 2001-516532        20000814
      EE 200200070         A     20030415    EE 2002-70            20000814
      US 6630503           B1    20031007    US 2000-638652        20000814
      NZ 517011            A     20040227    NZ 2000-517011        20000814
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	ZA 2002001158	A	20030512	ZA 2002-1158	20020211
	NO 2002000725	A	20020408	NO 2002-725	20020213
	BG 106510	A	20021031	BG 2002-106510	20020311
	US 2004132809	A1	20040708	US 2003-677756	20031003
PRAI	US 1999-148845P	P	19990813		
	US 2000-638652	A1	20000814		
	WO 2000-US22285	W	20000814		

OS MARPAT 134:193741

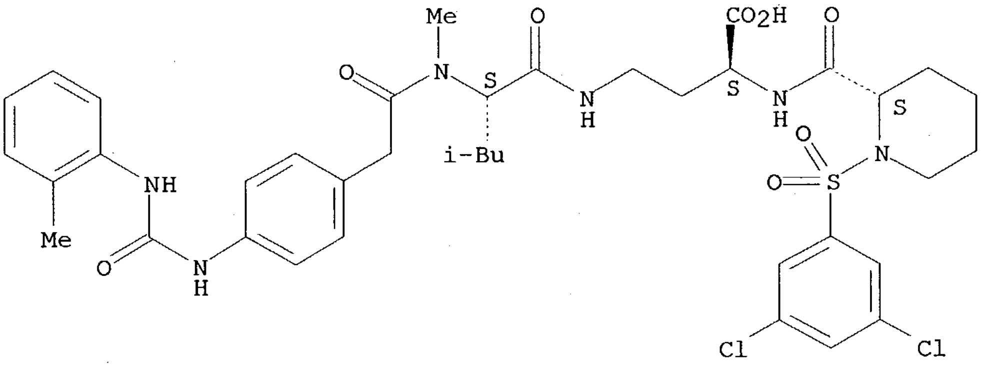
AB Cell adhesion inhibitors of the general formula R3-L-L'-R1 (R1 = H, C1-10alkyl, C2-10alkenyl or -alkynyl, cycloalkyl, cycloalkylalkyl, -alkenyl, or -alkynyl; L' and L are hydrocarbon linker moieties having 1-5 or 1-14 carbons, resp., which are optionally substituted and interrupted by, or terminally attached to, various groups; R3 = alkyl, cycloalkyl, aryl, aralkyl, aryloxy, arylamino, heterocyclyl, etc.) were prepared An inhibitor of the present invention interacts with VLA-4 mols. to inhibit VLA-4 dependent cell adhesion. Thus, N2-[N-[(3,5-dichlorophenyl)sulfonyl]-L-prolyl]-N4-[N-(o-MePUPA)-N-methyl-L-leucyl]-L-2,4-diaminobutyric acid [o-MePUPA = [4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl] was prepared via peptide coupling reactions in solution

IT **327613-21-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide derivs. as cell adhesion inhibitors)

RN 327613-21-8 CAPLUS

CN Butanoic acid, 2-[[[(2S)-1-[(3,5-dichlorophenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]-4-[[(2S)-4-methyl-2-[methyl[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-1-oxopentyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:354478 CAPLUS
DN 131:5529
TI Preparation of substituted β-alanine derivatives as cell adhesion inhibitors
IN Durette, Philippe L.; Hagmann, William K.; Kopka, Ihor E.; MacCoss, Malcolm; Mills, Sander G.; Mumford, Richard A.; Magriotis, Plato A.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

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     PATENT NO.          KIND  DATE        APPLICATION NO.        DATE
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PI   WO 9926921           A1   19990603    WO 1998-US24898        19981124
         W:  AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE,
             HR, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG,
             MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT,
             UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2309341           AA   19990603    CA 1998-2309341        19981124
     AU 9915327           A1   19990615    AU 1999-15327          19981124
     AU 751950            B2   20020905
     EP 1034164           A1   20000913    EP 1998-959547         19981124
     EP 1034164           B1   20040519
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
             SI, LT, LV, FI, RO
     JP 2001524465        T2   20011204    JP 2000-522079         19981124
     AT 267168            E    20040615    AT 1998-959547         19981124
PRAI US 1997-66484P       P    19971124
     GB 1997-27215        A    19971223
     WO 1998-US24898      W    19981124
OS   MARPAT 131:5529
GI
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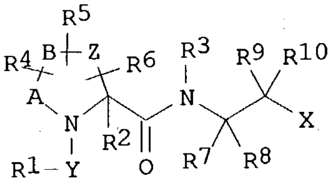
6,645,939



I

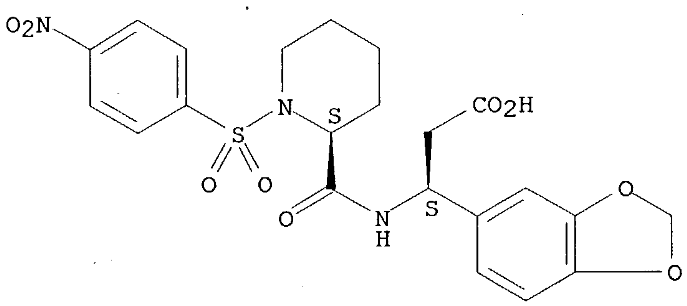
AB β-Alanine derivs. I [A, Z = C, C:C, C-C; B = a bond, C, C-C, C:C, N, O, S, S(O), SO2, N-Y-R1; X = CO2H, PO3H2, PH(O)OH, SO2H, SO3H or their esters or amides, 5-tetrazolyl; Y = CO, OCO, NHCO, SO2, etc.; R1 = (un)substituted alkyl, alkenyl, alkynyl, Cy (Cy = cycloalkyl, heterocycloalkyl, aryl, heteroaryl), Cy-alkyl, -alkenyl, or -alkynyl; R2 = H, (un)substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl; R3 = H, (un)substituted alkyl, Cy, Cy-alkyl; R4-R10 = H, alkyl, alkenyl, alkynyl, etc.] were prepared as antagonists of VLA-4 and/or α4β7 and as such are useful in the inhibition or prevention of cell adhesion and cell-adhesion mediated pathologies. Thus, N-[(3,4-dimethoxybenzenesulfonyl)-1,2,3,4-tetrahydroisoquinoline-3(S)-carbonyl]-3(S)-(3,4-methylenedioxyphenyl)-3-aminopropionic acid was prepared by amidation of N-(tert-butoxycarbonyl)-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid with Me (S)-3-amino-3-(3,4-methylenedioxyphenyl)propanoate, deblocking, sulfonylation with 3,4-dimethoxybenzenesulfonyl chloride, and saponification

IT **225515-74-2P 225516-38-1P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted β-alanine derivs. as cell adhesion inhibitors)

RN 225515-74-2 CAPLUS

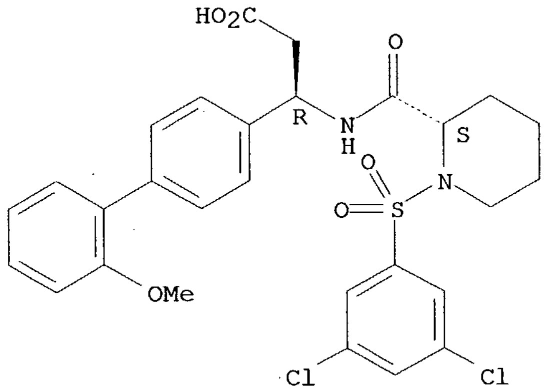
CN 1,3-Benzodioxole-5-propanoic acid, β-[[[(2S)-1-[(4-nitrophenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]-, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 225516-38-1 CAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, β-[[[(2S)-1-[(3,5-
dichlorophenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]-2'-methoxy-,
(βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:113711 CAPLUS
DN 130:153985
TI Preparation of N-sulfonylprolylphenylalanine derivatives and analogs as
inhibitors of leukocyte adhesion mediated by VLA-4
IN Thorsett, Eugene D.; Semko, Christopher M.; Pleiss, Michael A.; Lombardo,
Louis John; Konradi, Andrei W.; Grant, Francine S.; Dressen, Darren B.;
Dappen, Michael S.
PA Athena Neurosciences, Inc., USA; American Home Products Corporation
SO PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9906436	A1	19990211	WO 1998-US15327	19980731

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9885851          A1    19990222    AU 1998-85851          19980731
     EP 1001975          A1    20000524    EP 1998-937054         19980731
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     BR 9811573          A     20000919    BR 1998-11573          19980731
     JP 2001512138       T2    20010821    JP 2000-505191         19980731
     US 6362341          B1    20020326    US 1998-127601         19980731
     NO 2000000414       A     20000328    NO 2000-414            20000127
     US 2003065193       A1    20030403    US 2002-43275          20020114
     US 6586602          B2    20030701
PRAI US 1997-112007P     P     19970731
     US 1997-112007P     P     19970731
     US 1997-903585      A1    19970731
     US 1998-127601      A1    19980731
     WO 1998-US15327     W     19980731
OS   MARPAT 130:153985
AB   Disclosed are title compds. R1SO2NR2CHR3QCHR5COR6 [R1 = (un)substituted
     alkyl, (un)substituted aryl, (un)substituted cycloalkyl, (un)substituted
     heterocyclyl; R2NCHR3 form saturated heterocyclic group with the proviso that
     when monosubstituted, the substituent on the saturated heterocyclic group is
     not CO2H; R5 = (CH2)n-aryl, (CH2)n-heteroaryl; n = 1-4; Q = C(X)NR7; R7 =
     H, alkyl; X = O, S; R6 = NH2, (un)substituted alkoxy, (un)substituted
     cycloalkoxy, succinimidyloxy, adamantylamino, β-cholest-5-en-3-yloxy,
     NHOY, NH(CH2)pCO2Y, OCH2NR9R10; Y = H, (un)substituted alkyl,
     (un)substituted aryl; p = 1-8; R9 = (un)substituted CO-aryl; R10 = H,
     CH2CO2R11, NHSO2Z; R11 = alkyl; Z = (un)substituted alkyl, (un)substituted
     cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl,
     (un)substituted heterocyclyl; and pharmaceutically acceptable salts
     thereof, with the proviso that when R1 = 2,4,6-Me3C6H2, R2NCHR3 =
     pyrrolidinyl ring and Q = C(O)NH, then R5 ≠ benzyl; with the further
     proviso that when R1 = 4-MeC6H4, R2NCHR3 = pyrrolidinyl derived from
     D-proline, and Q = C(O)NH, then R5 ≠ benzyl derived from
     D-phenylalanine] which bind VLA-4 (also referred to as integrin
     α4β1 and CD49d/CD29).  Certain of these compds. also inhibit
     leukocyte adhesion and, in particular, leukocyte adhesion mediated by
     VLA-4.  Such compds. are useful in the treatment of inflammatory diseases
     in a mammalian patient, e.g., human, wherein the disease may be, for
     example, asthma, Alzheimer's disease, atherosclerosis, AIDS dementia,
     diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue
     transplantation, tumor metastasis and myocardial ischemia.  The compds.
     can also be administered for the treatment of inflammatory brain diseases
     such as multiple sclerosis.  Thus, BOP-mediated coupling of Boc-L-Pro-OH
     with L-phenylalanine benzyl ester hydrochloride in the presence of
     N-methylmorpholine, followed by acidic deprotection, sulfonylation with
     MeSO2Cl, and catalytic deprotection to give desired dipeptide
     MeSO2-L-Pro-L-Phe-OH.
IT   220186-90-3P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of N-sulfonylprolylphenylalanine derivs. and analogs as
        inhibitors of leukocyte adhesion mediated by VLA-4)
RN   220186-90-3  CAPLUS
CN   L-Phenylalanine, N-[[(2S)-1-[(4-methylphenyl)sulfonyl]-2-
     piperidinyl]carbonyl]- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
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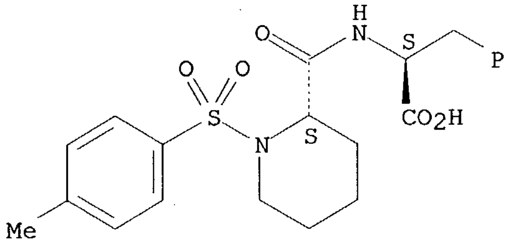

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RE.CNT  13     THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7   ANSWER 8 OF 11  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1998:799995  CAPLUS
DN   130:52736
TI   Preparation of biarylalkanoic acids as cell adhesion inhibitors
IN   Durette, Philippe L.; Hagmann, William K.; Maccoss, Malcolm; Mills, Sander
     G.; Mumford, Richard A.
PA   Merck & Co., Inc., USA
SO   PCT Int. Appl., 96 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE         APPLICATION NO.         DATE
     ---------------     ----   --------     --------------------    --------
PI   WO 9853817           A1    19981203     WO 1998-US10951         19980529
         W:  AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW,
             HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK,
             MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA,
             US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, ML, MR, NE, SN, TD, TG
     AU 9877031           A1    19981230     AU 1998-77031           19980529
     AU 726585            B2    20001109
     EP 1017382           A1    20000712     EP 1998-924988          19980529
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
     JP 2001517245        T2    20011002     JP 1999-500938          19980529
     US 6291511           B1    20010918     US 1999-359015          19990722
PRAI US 1997-47856P       P     19970529
     GB 1997-14316        A     19970707
     US 1997-66831P       P     19971125
     GB 1998-680          A     19980114
     US 1998-85793        B1    19980528
     WO 1998-US10951      W     19980529
OS   MARPAT 130:52736
AB   Compds. R1YNR2CR3R4CONR5CR6R7X [R1 = (un)substituted alkyl, alkenyl,
     alkynyl, a cyclic group Cy, Cy-alkyl, Cy-alkenyl, Cy-alkynyl; R2, R3
     independently are H or R1; or R2 and R3 together form a ring; R4, R7
     independently are H, (un)substituted alkyl, alkenyl, alkynyl, aryl,
     arylalkyl, heteroaryl, or heteroarylalkyl; or R3 and R4 together form a
     ring; R5 = H or (un)substituted alkyl or Cy; R6 = diarylalkyl, -alkenyl,
     or -alkynyl; X = CO2H, PO3H2, PH(O)OH, SO2H, SO3H or ester derivs.,
     carbamoyl group, or 5-tetrazolyl; Y = CO, OCO, NHCO or iminocarbonyl
     group, SO2, P(O)(ORi) (Ri =alkyl, alkenyl, alkynyl, aryl), COCO] were
     prepared as cell adhesion inhibitors.  Pharmaceutical compns. are described.
     Thus, N-(3,5-dichlorobenzenesulfonyl)-L-prolyl-L-4-(4-
     fluorophenyl)phenylalanine was prepared by coupling of N-(3,5-
     dichlorobenzenesulfonyl)-L-proline with 4-iodo-L-phenylalanine and
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         reaction with 4-fluorobenzeneboronic acid.
IT       217326-25-5P
         RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
         study); PREP (Preparation); USES (Uses)
            (preparation of peptidyl biarylalkanoic acids as cell adhesion inhibitors)
RN       217326-25-5  CAPLUS
CN       [1,1'-Biphenyl]-4-propanoic acid, 2'-cyano-α-[[[(2S)-1-[(3,5-
         dichlorophenyl)sulfonyl]-2-methyl-2-piperidinyl]carbonyl]amino]-,
         (αS)- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
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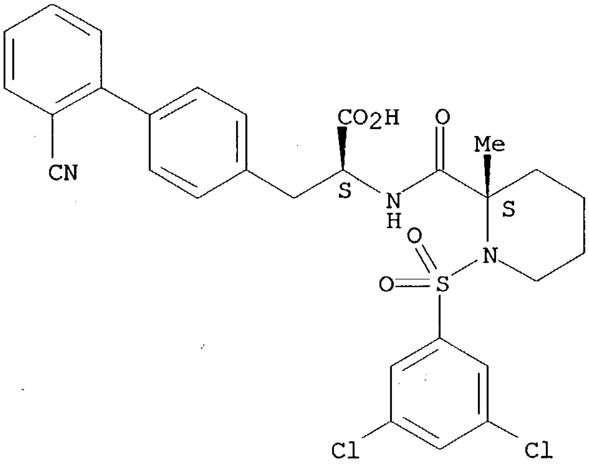

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RE.CNT  1       THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
                ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7     ANSWER 9 OF 11  CAPLUS  COPYRIGHT 2004 ACS on STN
AN     1998:799992  CAPLUS
DN     130:52724
TI     Preparation of heterocyclic dipeptide derivatives as cell adhesion
       inhibitors
IN     Durette, Philippe L.; Hagmann, William K.; Maccoss, Malcolm; Mills, Sander
       G.; Mumford, Richard A.; Van Riper, Gail M.; Schmidt, Jack A.; Kevin,
       Nancy J.
PA     Merck & Co., Inc., USA
SO     PCT Int. Appl., 129 pp.
       CODEN: PIXXD2
DT     Patent
LA     English
FAN.CNT 1
       PATENT NO.          KIND   DATE        APPLICATION NO.      DATE
       ---------------     ----   --------    --------------------  --------
PI     WO 9853814           A1    19981203    WO 1998-US10940      19980529
           W:  CA, JP, US
           RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
               PT, SE
       EP 1001764           A1    20000524    EP 1998-926122       19980529
           R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
       JP 2002512625        T2    20020423    JP 1999-500934       19980529
       WO 9964395           A1    19991216    WO 1998-US11623      19980611
           W:  AL, AM, AU, AZ, BA, BB, BG, BR, BY, CN, CU, CZ, EE, GE, GW, HU,
               ID, IL, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX,
               NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN,
               YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
           RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA,
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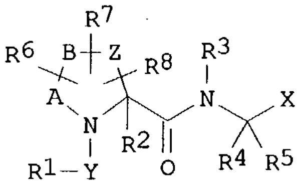
GN, ML, MR, NE, SN, TD, TG

	AU 9880595	A1	19991230	AU 1998-80595	19980611
PRAI	US 1997-48017P	P	19970529		
	GB 1997-14314	A	19970707		
	US 1997-66525P	P	19971125		
	GB 1998-686	A	19980114		
	WO 1998-US10940	W	19980529		
	WO 1998-US11623	A	19980611		

OS MARPAT 130:52724

GI



I

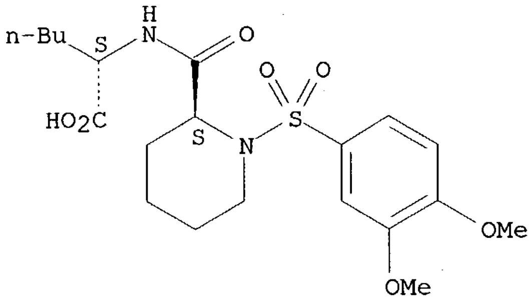
AB Title compds. I [R1 = (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, Cy, Cy-C1-10 alkyl, Cy-C2-10 alkenyl, Cy-C2-10 alkynyl; R2, R5 = independently (un)substituted H, C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, aryl, aryl-C1-10 alkyl, heteroaryl, heteroaryl-C1-10 alkyl; R3 = H, (un)substituted C1-10 alkyl, Cy, Cy-C1-10 alkyl; R4 = H, any group R1; R3R4 form mono- or bicyclic ring containing 0-2 heteroatoms N, O, S; R4R5 form 3-7 membered mono- or bicyclic ring containing 0-2 heteroatoms N, O, S; R10, R11 = independently = any group R3, (un)substituted C2-10 alkenyl, C2-10 alkynyl; R10R11 may form 5-7 membered heterocyclic ring containing 0-2 addnl. heteroatoms N, O, S; R6-R8 = independently any group R10, OR10, NO2, halo, S(O)mR10, SR10, SO3R10, NR10R11, COR10, CO2R10, O2R10, CN, CONR10R11, CF3, oxo, NR10S(O)mR11, etc.; two of R6-R8 may form 5-7 membered (un)saturated monocyclic ring containing 0-3 heteroatoms N, O, S; Cy = cycloalkyl, heterocyclyl, aryl, heteroaryl; A, Z = independently C, C-C; B = bond, C, C-C, N, O, S, S(O)m; X = CO2R10, P(O)(OR10)(OR11), P(O)(R10)(OR11), S(O)mOR10, CONR10R11, 5-tetrazolyl; Y = CO, O2C, NR11CO, SO2, P(O)(OR4), COCO; m = 1-2] = are antagonists of VLA-4 and/or α4β7, and are useful for inhibition or prevention of cell adhesion and cell adhesion mediated pathologies. These compds. may be formulated into pharmaceutical compns. and are suitable for use in the treatment of asthma, allergies, inflammation, multiple sclerosis, and other inflammatory and autoimmune disorders. Thus, coupling of L-2-naphthylalanine tert-Bu ester (H-Nal-OtBu) (preparation given) with Cbz-Pro-OH (Cbz = PhCH2O2C), followed by catalytic deprotection, sulfonylation with 3,5-Cl2C6H3SO2Cl, and acidic deesterification gave desired N-sulfonyldipeptide Cl2C6H3SO2-Nal-Pro-OH. Procedures for inhibition of VLA-4 dependent adhesion to a CS-1 conjugate and VCAM-IG fusion protein are given.

IT **217450-99-2P 217451-00-8P 217451-01-9P**
217451-02-0P 217451-03-1P 217451-05-3P
217451-06-4P 217451-21-3P 217451-28-0P
217451-36-0P 217452-40-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic dipeptide derivs. as cell adhesion inhibitors)

RN 217450-99-2 CAPLUS

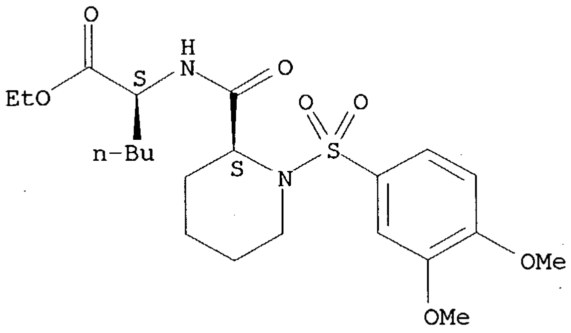
CN L-Norleucine, N-[[(2S)-1-[(3,4-dimethoxyphenyl)sulfonyl]-2-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



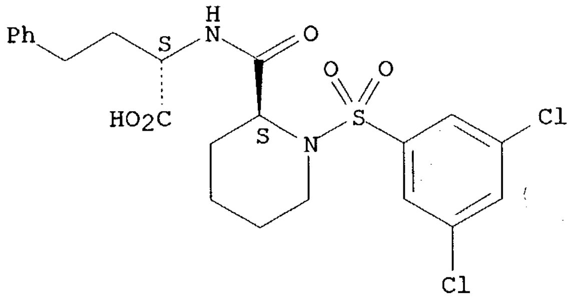
RN 217451-00-8 CAPLUS
CN L-Norleucine, N-[[(2S)-1-[(3,4-dimethoxyphenyl)sulfonyl]-2-piperidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



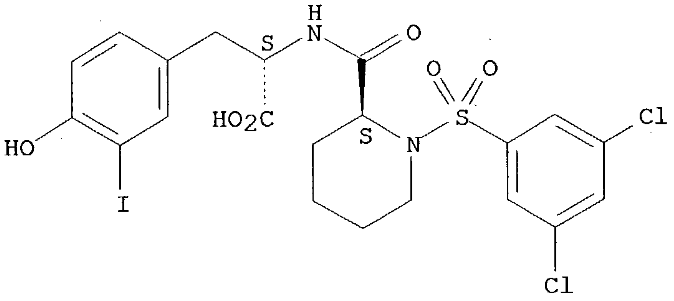
RN 217451-01-9 CAPLUS
CN Benzenebutanoic acid, α-[[[(2S)-1-[(3,5-dichlorophenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



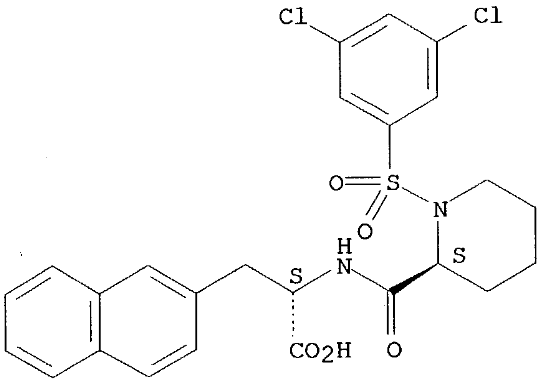
RN 217451-02-0 CAPLUS
CN L-Tyrosine, N-[[(2S)-1-[(3,5-dichlorophenyl)sulfonyl]-2-piperidinyl]carbonyl]-3-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



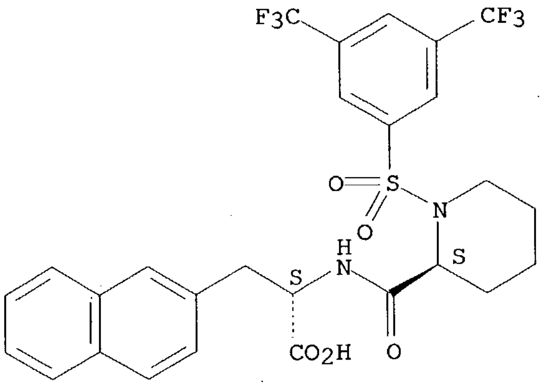
RN 217451-03-1 CAPLUS
CN 2-Naphthalenepropanoic acid, α-[[[(2S)-1-[(3,5-dichlorophenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



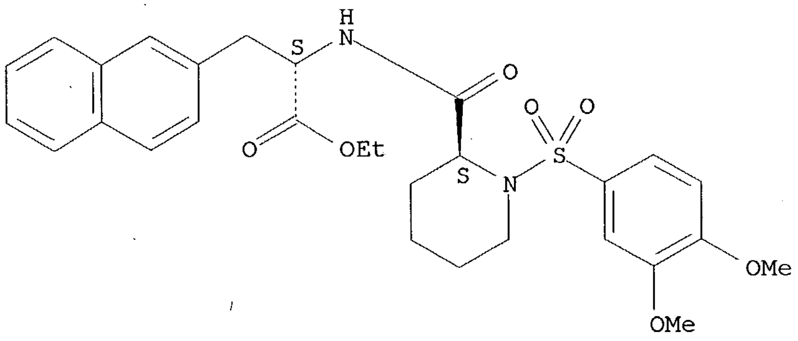
RN 217451-05-3 CAPLUS
CN 2-Naphthalenepropanoic acid, α-[[[(2S)-1-[[3,5-bis(trifluoromethyl)phenyl]sulfonyl]-2-piperidinyl]carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



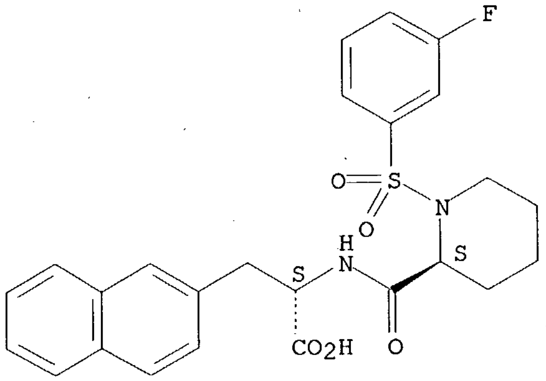
RN 217451-06-4 CAPLUS
CN 2-Naphthalenepropanoic acid, α-[[[(2S)-1-[(3,4-dimethoxyphenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]-, ethyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



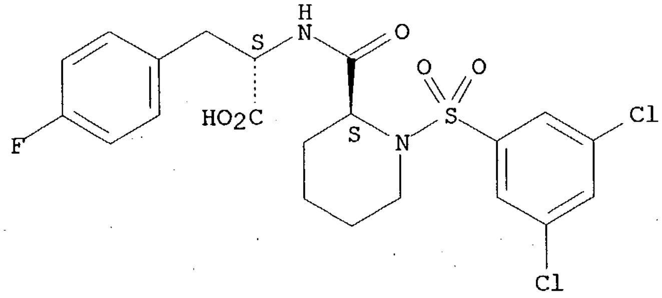
RN 217451-21-3 CAPLUS
CN 2-Naphthalenepropanoic acid, α-[[[(2S)-1-[(3-fluorophenyl)sulfonyl]-2-piperidinyl]carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



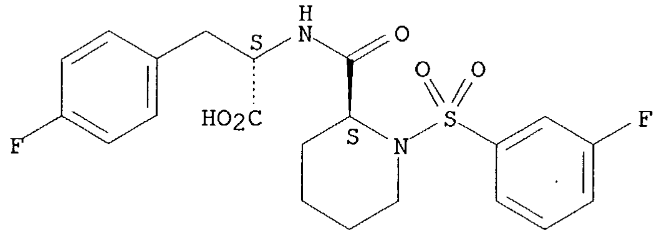
RN 217451-28-0 CAPLUS
CN L-Phenylalanine, N-[[(2S)-1-[(3,5-dichlorophenyl)sulfonyl]-2-piperidinyl]carbonyl]-4-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 217451-36-0 CAPLUS
CN L-Phenylalanine, 4-fluoro-N-[[(2S)-1-[(3-fluorophenyl)sulfonyl]-2-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

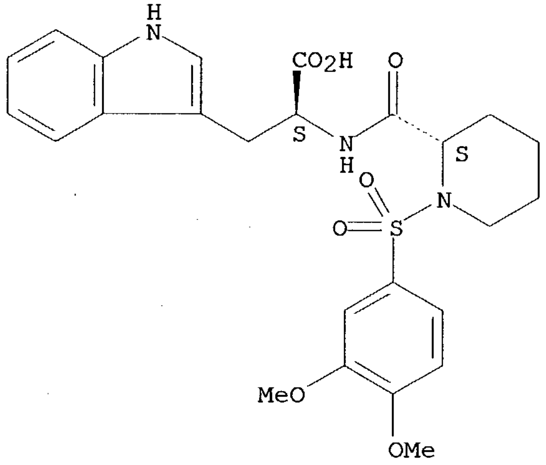
Absolute stereochemistry.



RN 217452-40-9 CAPLUS

CN L-Tryptophan, N-[[(2S)-1-[(3,4-dimethoxyphenyl)sulfonyl]-2-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

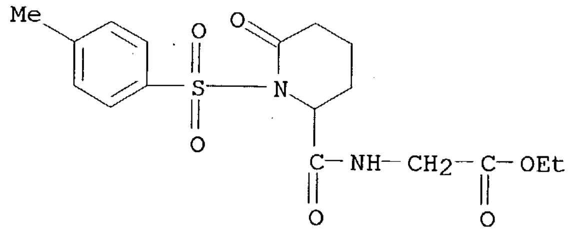
L7 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1964:31347 CAPLUS
DN 60:31347
OREF 60:5630f-h,5631a-d
TI New methods for the synthesis of derivatives and peptides of α-aminoadipic acid
AU Gut, V.; Rudinger, J.
CS Ceskoslov. Akad. Ved, Prague
SO Collection of Czechoslovak Chemical Communications (1963), 28(11), 2953-68
CODEN: CCCCAK; ISSN: 0010-0765
DT Journal
LA English
OS CASREACT 60:31347
GI For diagram(s), see printed CA Issue.
AB Syntheses of title compds. are described via 6-oxo-1-tosyl-L-piperidine-2-carboxylic acid (I) and (R)-4-(5-oxo-3-tosyloxazolidin-4-yl)butyric acid (II) as the key intermediates. Thus, 9.45 g. tosyl-L-α-aminoadipic acid (IIa) in 70 ml. dry pyridine treated with 6.85 g. p-MeC6H4SO2Cl in 60 ml. Et2O gave 7.46 g. I, m. 200-1° (dioxane-C6H6-petr. ether), [α]20D 39.6° (c 3.37, 98% AcOH); Me ester m. 109-10° (60% EtOH); Et ester m. 101-2° (EtOH). Refluxing 1.48 g. I with 30 ml. concentrated aqueous NH4OH for 15 min. gave 1.49 g. tosyl-L-α-aminoadipic acid δ-amide (III), m. 226-8°, [α]2D5 4.7° (c 0.231, 98% AcOH), identical with the product obtained in 1.75 g. from 2.52 g. IIa via the acid chloride. Hofmann degradation of III with NaOBr in

10% NaOH gave Nα-tosyl-L-ornithine, m. 186-8° (decomposition). Evaporating 2.97 g. I in 3.05 ml. 40% aqueous N2H2 at 40° in vacuo gave 3.18 g. tosyl-L-α-aminoadipic acid δ-hydrazide (IV), m. 186-9°, yielding, after Curtius degradation, 29% (R)-3-tosylaminopiperid-2-one, m. 183-4°. I (2.97 g.) and 3.09 g. NH2CH2CO2Et heated in 2.5 ml. Me2SO 1 hr. at 95-100°, the mixture poured into 100 ml. 10% HCl, and kept 12 hrs. at 0° gave 2.52 g. δ-(tosyl-L-α-aminoadipyl)glycine Et ester (V), m. 154-5° (aqueous EtOH), identical with the product obtained in 43%, yield from IV by azide synthesis. Saponification of 2.16 g. V in 4.2 ml. 4N NaOH gave 1.76 g. δ-(tosyl-L-α-aminoadipyl)glycine (VI), m. 116-18°, [α]20D 7.2° (c 3.13, 98% AcOH). I (2.97 g.) refluxed with 4 ml. SOCl2 until all dissolved and the solution evaporated to dryness gave 2.87 g. 6-oxo-1-tosyl-L-piperidine-2-carboxylic acid chloride (VII), m. 154-5° (C6H6-Et6O). Treatment of 316 mg. VII with excess NH3 in CHCl3 gave 243 mg. 6-oxo-1-tosyl-L-piperidine-2-carboxamide, m. 255-8° (aqueous AcOH), which yielded, when shaken 3 hrs. with 4N NaOH, a mixture of approx. equal parts of L-α-aminoadipic acid δ-amide (VIII) and L-α-aminoadipic acid δ-amide (IX), and, when heated with NH3-saturated HCONH2 in an autoclave contg, liquid NH3 3 hrs. at 100°, 90% tosyl-L-α-aminoadipic acid diamide, m. 225-40° (decomposition). Shaking 1.89 g. VII in 12 ml. CHCl3 with 0.84 g. NH2CH2CO2Et. HCl, 1.1 g. NaHCO3, and 5 ml. H2O until evolution of COs ceased gave 2 g. IXa, m. 137-9° (EtOH), which was kept in 4N NaOH 1 hr. to give 90% α-(tosyl-L-α-aminoadipyl)glycine (X), m. 165-6° (H2O), [α]25D -7.7° (c 0.010, 98% AcOH), and about 3% of the δ-isomer, determined by chromatography after reduction with Na in liquid NH3. An alternative approach was examined, starting from II. IIa (10 g.) and 1.9 g. paraformaldehyde in 64 ml. hot AcOH was heated with 3 ml.Ac2O and 3 drops SOCl2 4 hrs. on a water bath to give 9.8 g. II.C6H6, m. 56-8°. Boiling 1 g. II.C6H6 briefly with 10 ml. concentrated aqueous NH4OH gave 0.64 g. tosyl-L-α-aminoadipic acid α-amide (XI), m. 215-18° (aqueous EtOH), [α]20D -9.0° (c 0.234, 98% AcOH). II (1 g.) heated 2 min. at 100° with 1.3 g. NH2CH2CO2Et gave 1.03 g. α-(tosyl-L-αaminoadipyl)glycine Et ester, m. 124° (EtOH-H2O). Refluxing 4.5 g. II 10 min. with 10 ml. SOCl2 gave 3.9 g. (R)-4-(5-oxo-3tosyloxazolidin-4-yl)butyryl chloride (XIa), m. 76-8° (C6H6), which was treated at -20° with M NH3 in CHCl3 to give 97% (R)4-(5-oxo-3-tosyloxazolidin-4-yl)butyramide (XII), m. 132-4° (iso-PrOH). XII kept 1 hr. with 4N NaOH gave 44% III. XIa shaken with NH2CH2CO2Et.HCl, NaHCO3, CHCl3, and H2O gave an oily oxazolidone ester, which was sapond, with 4N NaOH in MeOH to VI. III (494 mg.) was treated with Na in 50 ml. liquid NH3 to give 140 mg. VIII, m. 179-81° (decomposition), [α]26D 21.3° (c 2.14, N HCl), also obtained in 0.23-g. yield by heating 550 mg. III with a 35% solution of HBr in 5 ml. AcOH containing 0.2 g. PhOH 24 hrs. at 40°. Similarly, reduction of 417 mg. XI with Na in liquid NH3 gave 144 mg. IX, m. 166-8° (aqueous EtOH), [α]20D 20.8° (c 0.56, N HCl), and VI and X yielded, by the same technique, 75% δ-(L-α-aminoadipyl)glycine [NH4 salt m. 185-90°; free peptide m. 194-5°, [α]20D 16.0° (c 4.5, N HCl), 4.7° (c 0.78, H2O)], and 69% α-(L-α-aminoadipyl)glycine [NH4 salt, [α]2D0 36.4° (c 3.84, N HCl)], resp.

IT **98074-96-5**, Glycine, N-[6-oxo-1-(p-tolylsulfonyl)pipecoloyl]-, ethyl ester
(preparation of)

RN 98074-96-5 CAPLUS

CN Glycine, N-[6-oxo-1-(p-tolylsulfonyl)pipecoloyl]-, ethyl ester (7CI) (CA INDEX NAME)



L7 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1962:469511 CAPLUS
DN 57:69511
OREF 57:13878c-i,13879a-i,13880a-b
TI Participation of isolated double bonds in cleavage of peptides with N-bromosuccinimide
AU Izumiya, Nobuo; Francis, John E.; Robertsou, Alexander V.; Witkop, Bernhard
CS Natl. Insts. of Health, Bethesda, MD
SO Journal of the American Chemical Society (1962), 84, 1702-9
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA Unavailable
OS CASREACT 57:69511
GI For diagram(s), see printed CA Issue.

AB N-Acylated amides and peptides derived from DL-2-amino-4-pentenoic acid (I), DL-2-amino-4-methyl-4-pentenoic acid (II), DL-baikiain (III), and 3,4-dehydro-DL-proline (IV) were synthesized and studied with regard to participation of the double bond in displacement reactions with N-bromosuccinimide (V). Three different reaction types were observed: (1) the pentenoic acid amides and peptides released NH3 or glycine (VI) in high yield via isolable dibromoiminolactone and C-bromolactone intermediates, resp.; (2) the amide of III produced 2-oxa-3-bromoimino-5-tosylaza-7-bromobicyclo[3.2.1]octane (VII), which was only slowly hydrolyzed to yield NH3. No reaction occurred between V and the baikiain peptide. (3) No participation of the β,γ-double bond in IV was observed. However, NH3 was released at pH 6 from acyldehydroprolinamides probably via an unusually easy Hofmann rearrangement. The remarkable dicarbinolamide VIII was isolated from the reaction of Ncarbobenzyloxydehydroprolinamide (IX) with V. The pH profiles of these cleavage reactions were determined and were of diagnostic value in recognizing the nature and location of the double bond in peptides and amides derived from unsatd. amino acids. Carbobenzyloxylation: A. The solution of IV (1.13 g.) in 50 ml. H2O and 10 ml. N NaOH was cooled to its freezing point and 2 ml. carbobenzoxy chloride (X) in 10 ml. Et2O added, 1N NaOH added to keep the pH at 9-10, after 40 min. the solution extracted with Et2O, the aqueous fraction acidified, and the oil extracted with EtOAc to give 2.4 g. of a gum. Attempts to effect crystallization were unsuccessful. The oil was N-carbobenzyloxy-3,4-dehydro-DL-proline (XI). XI was used directly for the preparation of N-carbobenzyloxy3,4-dehydroprolylglycine (XII). 3,4-Dehydro-DL-prolin-amide (1.12 g.) in 25 ml. 2N NaOH cooled to -10°, treated 0.5 hr. with 2 ml. X, and the product crystallized gave 2.05 g. IX, m. 132-3°. All amino acids were benzoylated in NaOH with BzCl by the Schotten-Baumann procedure. III.HCl (818 mg.) in 30.9 ml. 0.3N NaOH stirred with 1 g. p-MeC6H4SO2Cl, after 6 hrs. the mixture filtered, acidified, extracted with EtOAc, and the product isolated gave 1.215 g. oil, N-tosyl-DL-baikiain. Solns. of the N-acylated amino acids in organic solvent were converted to the Me esters by reaction with CH2N2 in Et2O. The ester in MeOH was saturated with NH3 at 0°. The reaction was usually left 1-2 days at room temperature Preparation of peptides: The acylated amino acid was treated with an appropriate amino acid ester or its salt, such as the Et ester HCl salt of VI, in an organic solvent with dicyclohexylcarbodiimide and NEt3. Reaction times varied from a few hrs. to 2 days at room temperature or 0°. In some cases the mixed anhydride method gave good results. The N-acyl peptide esters were converted to the crystalline N-acyl peptides by the action of one equivalent NaOH in aqueous MeOH at room temperature The saponification reaction was allowed to proceed 12-24 hrs. In the following expts., the amide or peptide (0.2 millimole) was dissolved in 5 ml. MeCN and 5 ml. buffer solution and diluted with H2O. V was dissolved in H2O. Theread following procedure was carried out: (1) 10 ml. of the amide or peptide solution placed in each of 8 flasks; (2) to one of each of the flasks was added the following vols. of V solution: 0.0 ml., 0.3, 0.6, 1.0, 1.5, 2.0, 2.5, and 3.0 ml.; (3) after 10 min. the solns. were made up with H2O; (4) 1 ml. portions of each were shaken with ninhydrin solution; (5) the tubes were heated 15 min., cooled, and treated with 8 ml. 50% aqueous PrOH, then shaken and the density read. In the 1st expts. the zero reading was taken with the tube containing 50% PrOH, and all the readings calculated on the basis of this value. Various buffer solns. were prepared from reactions carried out at different pH values. DL-Benzamido-4-pentenoylglycine (XIII) (0.276 g.) in 20 ml. MeCN and 20 ml. H2O left 1 hr. with 0.187 g. V in 40 ml. H2O, the mixture evaporated, and the filtrate extracted with EtOAc, the aqueous layer set aside, the organic layer washed, evaporated, and the residue recrystd. gave 0.125 g. 2-benzamido4-hydroxy-5-bromopentanoic acid lactone (XIV), m. 161-2° (EtOAc-ligroine). XIV was also obtained from the interaction of V and DL-2-benzamido-4-pentenoic acid (XV) under these conditions. The yield was 31%. The aqueous layer containing VI was evaporated, washed with EtOAc, dissolved in H2O containing 0.5 ml. NEt3, the solution evaporated, and the residue washed to give 55% VI, m. 250-2° (decomposition). DL-2-p-Toluenesulfonamido-4-pentenoylglycine (XVI) (0.326 g.) was treated with V as above; the oily crude lactone solidified after several days and the product was crystallized to give 0.145 g. 2-p-toluenesulfonamido-4-hydroxy-5-bromopentanoic acid lactone, m. 134-5°. As above, 56% VI was isolated from the aqueous phase. DL-2-Benzamido-4methyl-4-pentenoylglycine (XVII) (0.145 g.) cleaved with V as above, and the lactone isolated gave 0.058 g. 2-benzamido-4-hydroxy-4-methyl-5-bromopentanoic acid lactone, m. 173-4°. VI was obtained in 59% yield from the aqueous layer. DL-2-Benzamido-4-pentenoic acid amide (XVIII) (1 g.) in 100 ml. hot MeCN left 4 hrs. in a refrigerator with 1.8 g. V gave 1 g. 2-bromoimino-3-benzamido-5-bromomethyltetrahydrofuran (XIX), m. 125-7°. Aliquots of XIX in 1:9 MeCN-H2O released 100% of the imino-N as NH3. XIX (100 mg.) refluxed 2 hrs. in 10 ml. MeCN-H2O gave 75 mg. XIV. DL-2-Benzamido-4-methyl-4-pentenoic acid amide (XX) (0.116 g.) treated with 0.095 g. V gave 15% 2-bromoimino-3-benzamido-5-methyl-5-bromomethyltetrahydrofuran, m. 141-4°. DL-2-p-Toluenesulfonamido-4methyl-4-pentenoic acid amide (XXI) (0.085 g.) with 0.057 g. V gave 12% 2-bromoimino-3-p-toluenesulfonamido-5methyl-5-bromomethyltetrahydrofuran, m. 124-6° (decomposition). N-Tosyl-DL-baikiain amide (XXII) (280 mg.) in 25 ml. warm MeCN added to 400 mg. V in 100 ml. H2O and the product isolated after 2 hrs. at 0° gave 350 mg. VII, m. 142-3°. VII in MeCN-H2O gave a ninhydrin color yield of 15% after 15 min. at 100° and 20% after 1 hr. VII (300 mg.) refluxed 1 hr. in 10 ml. 90% AcOH, the liberated Br evaporated, the solvent removed, and the residue distributed between EtOAc and H2O gave 95 mg. N-tosyl-4-hydroxy-5bromopipecolic acid lactone, m. 179-81°. The bicarbonate layer acidified and the precipitate extracted with EtOAc gave 100 mg. N-tosyl-4-hydroxy-5-bromopipecolic acid, m. 193-5° (EtOAc-CHCl3). Preliminary expts. showed that the above reaction conditions were necessary for complete hydrolysis and also gave the maximum yield of lactone. Over 60% of VII remained when it was treated under the conditions which effected complete hydrolysis of XIX. Thus the following derivs. of I-IV were prepared and cleaved (compound, crystal form, solvent, m.p., and % yield given): XV, plates, EtOAc-ligroine, 107-8°, 86; XVIII, plates, MeOH-ligroine, 175°, 77; DL-2-benzamido-4-pentenoylgtycine benzyl ester, -, EtOAc-ligroine, 106-8°, 77; XIII, -. Me2CO-ligroine, 126 9°, 90; DL-2-benzamido-4-pentenoylglycinamide, -, EtOAc-ligroine, 137-8°, 85; DL-2-p-toluenesulfonamido-4pentenoic acid, prisms, Et2O-ligroine, 100-1°, 89: DL-2-ptoluenesulfonamido-4-pentenoic acid amide, hexagonal prisms, MeOH-Me2CO, 192-3°, 56; XVI, -, Me2COEt2O, 134-6°, 85; DL-2-benzamido-4-methyl-4-pentenoic acid, plates, EtOAc-ligroine, 135-6°, 78; XX, plates, MeOH- ligroine, 176°, 78; DL-2-benzamido-4-methyl-4-pentenoylglycine benzyl ester, -, EtOAc-ligroine, 123-5°, 74; XVII, -, alc.-ligroine, 200°, 67; DL-2-p-toluenesulfonamido-4-methyl-4-pentenoic acid, -, Et2O-ligroine, 11214°, 82; DL-2-p-toluenesulfonamido-4-methyl-4-pentenoic acid Me ester, -, Et2O-ligroine, 81-3°, 72; XXI, prisms, MeOH-ligroine, 182-4°, 48; DL-2-p-toluenesulfonamido-4methyl-4-pentenoylglycine, -, EtOAc-ligroine, 164-6°, 74; benzoyl-3,4-dehydro-DL-proline, prisms, Me2CO-Et2O, 137-41°, 90; benzoyl-3,4-dehydro-DL-prolinamide, plates, H2O, 189-91°, 80; benzoyl-3,4-dehydro-DL-prolylglycine, -, alc.-ligroine, 160-1°, 60; IX, -, C6H6; 132-3°, 83; XII, -, alc.-EtOAc, 168.5-9.5°, 60; tosyl-3,4-dehydroDL-proline, prisms, CH2Cl2-ligroine, 141-4°, 100; tosyl-3,4dehydro-DL-proline Me ester, -, MeOH-ligroine, 97.58.5°, 94; tosyl-3,4-dehydro-DL-prolinamide, hexagonal prisms, MeOH, 202-4°, 83; tosyl-3,4-dehydro-DL-prolylglycine Et ester, -, EtOAc-ligroine, 84-5°, 69; tosyl-3,4dehydro-DL-prolylglycine, -, alc.-Et2O, 236-7°, 70; tosylDL-baikiain Me ester, hexagonal prisms, Et2O-ligroine, 76-6.5°, 60; XXII, prisms, MeOH, 169-70°, 42; tosyl-4,5-dehydro-DL-pipecolylglycine, -, Me2CO-Et2O, 167-8°, 57; acetyl-L-phenylalaninamide, -, alc.-Et2O, 182-3°, 83; acetyl-DL-phenylalanylglycine benzyl ester, -, alc.-ligroine, 143°, 70; acetyl-DL-phenylalanylglycine, prisms, MeOH-ligroine, 179-80°, 80.

IT **97469-11-9**, Glycine, N-[1,2,3,6-tetrahydro-1-(p-tolylsulfonyl)picolinoyl]-
(preparation of)

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CN Glycine, N-[1,2,3,6-tetrahydro-1-(p-tolylsulfonyl)picolinoyl]- (7CI) (CA INDEX NAME)